

### **REMARKS**

The present invention relates to regulatory T cells (Treg cells) and methods of long-term, culture-expanding, activating and using same in immunotherapy and for the suppression of autoimmune responses.

By way of the present Amendment, claims 6 and 12-27 have been canceled, and claims 1, 4, 5, 7, 8, 10 and 28 have been amended. Specifically, claims 1, 4 and 28 have been amended for clarity as suggested by the Examiner.

Claim 1 has been amended to incorporate the limitations of claims 5 and 27. Claim 27 was not rejected as being anticipated or obvious over the cited art. Accordingly, it is believed that the amendment to claim 1 wherein it recites "activating the isolated CD4<sup>+</sup>CD25<sup>+</sup> cells with beads coated with anti-CD3 and anti-CD28 antibodies at a ratio of a higher amount of anti-CD28 antibody to anti-CD3 antibody" places claim 1 in condition for allowance.

Claims 5, 7, 8, 10 and 28 have been amended to be consistent with the above-noted claim cancellations and amendments.

Applicants appreciate the time taken by the Examiner during the telephone interview that took place on September 6, 2007, with Applicants' representative, Kathryn Doyle (the undersigned). During the telephone interview, Applicants agreed to amend the claims to clarify the purification process.

### **Revocation and Appointment of Attorney by Assignee**

As discussed in the interview held on September 6, 2007, kindly note that the undersigned, Attorney for Applicants, is counsel for Applicants in connection with the above-captioned application. A Revocation and Appointment of Attorney by Assignee has filed on January 9, 2007, a copy of which is enclosed herewith for the Examiner's convenience. It is requested that any future communications from the Patent Office be sent to the undersigned at the following address:

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#### Objection to claim 28

The Examiner has objected to claim 28 because the word "ratio" appears to have been omitted.

In response, claim 28 has been amended to state that "the ratio of anti-CD3 antibody to anti-CD28 antibody is at least 1:5".

#### Response to Rejections Under 35 U.S.C. 112, Second Paragraph

Claims 1-11 and 27-29 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for reciting the phrases "using a lower titer of anti-CD25" and "modified magnetic antibody cell sorting". The Examiner contends that the metes and bounds of "lower titer" is not clear and that the skilled artisan would not know how the "modified magnetic antibody cell sorting" procedure is modified.

In response, Applicants have amended claim 1 to remove the recitation of "a lower titer" and the word "modified". In addition, claim 1 has been amended to recite "anti-CD25 magnetic microbeads" to clarify the identity of the anti-CD25 entity as per the Examiner's suggestion. Applicants respectfully submit that the amendments to claim 1 make it definite.

In addition to the amendments to claim 1, Applicants have amended claim 4 to be consistent with the amendments to claim 1 and to recite that the anti-CD25 magnetic microbeads are used at less than 10 $\mu$ l per 10<sup>7</sup> cells.

Support for the above amendments is found through out the specification. For example, Example 8 (specifically in paragraph [0185]) discloses that CD25<sup>+</sup> cells were isolated by positive selection from peripheral blood mononuclear cells (PBMC) using anti-CD25 magnetic microbeads at an amount that is less than 10 $\mu$ l per 10<sup>7</sup> cells (2  $\mu$ l per 10<sup>7</sup> cells) (Miltenyi Biotec, Auburn, Calif.), and purified over a magnetic column. The cells were then applied to a second magnetic column, washed, and re-eluted.

Accordingly, Applicants respectfully request that the rejection of claims 1-11 and 27-29 under 35 U.S.C. § 112, second paragraph, as being indefinite be reconsidered and withdrawn. Furthermore, Application contend that claim 1 and dependent claims therefrom fully comply with the standards set forth under 35 U.S.C. § 112, second paragraph.

Rejection of claims 1-4, 11 and 26 pursuant to 35 U.S.C. §102(e), or in the alternative pursuant to 35 U.S.C. §103(a)

The Examiner has rejected claims 1-4, 11 and 26 under 35 U.S.C. § 102(e) as being anticipated by Schuler et al. (U.S. Patent Application Pub. No. 2005/0101012) as evidenced by the CD25 MicroBeads magnetic cell sorting protocol and the CD8 Microbead online product literature, or in the alternative, under 35 U.S.C. §103(a) as obvious over Schuler in view of the MicroBead magnetic cell sorting protocols.

Solely in order to expedite prosecution of the present application, Applicants have canceled independent claim 26 and have amended claim 1 to incorporate the limitation of claim 27, which was not rejected as being anticipated or obvious over Schuler et al. in view of the CD25 MicroBead protocol.

Specifically, amended claim 1 recites that the culture-expanding step includes "activating the isolated CD4<sup>+</sup>CD25<sup>+</sup> cells with beads coated with anti-CD3 and anti-CD28 antibodies at a ratio of a higher amount of anti-CD28 antibody to anti-CD3 antibody".

In view of this amendment, Applicants respectfully submit that claim 1, the only independent claim pending and under examination in the present application, is not anticipated or rendered obvious by Schuler et al. in view of the cited MicroBeads magnetic cell sorting protocols. Withdrawal of this rejection is thus respectfully requested.

Rejection of claims 1-3, 5, 11 and 29 pursuant to 35 U.S.C. §102(e), or in the alternative pursuant to 35 U.S.C. §103(a)

The Examiner has rejected claims 1-3, 5, 11, and 29 under 35 U.S.C. § 102(e) as being anticipated by Roncarolo et al. (US2004/0173778), or in the alternative, under 35 U.S.C. 103(a) as obvious over Roncarolo in view of the CD25 MicroBead protocol.

As indicated above, solely to expedite prosecution of the present application, Applicants have amended claim 1 to incorporate the limitation of claim 27, which was not rejected as being anticipated or obvious over Roncarolo et al. in view of the CD25 MicroBead protocol.

Specifically, amended claim 1 recites that the culture-expanding step includes "activating the isolated CD4<sup>+</sup>CD25<sup>+</sup> cells with beads coated with anti-CD3 and anti-CD28 antibodies at a ratio of a higher amount of anti-CD28 antibody to anti-CD3 antibody".

In view of this amendment, Applicants respectfully submit that claim 1, the only independent claim pending and under examination in the present application, is not anticipated or rendered obvious by Roncarolo et al. in view of the cited MicroBead magnetic cell sorting protocols. Withdrawal of this rejection is thus respectfully requested.

Rejection of claims 6-10 pursuant to 35 U.S.C. §103(a)

The Examiner has rejected claims 6-10 under 35 U.S.C. § 103(a) as being unpatentable over Roncarolo et al. in view of Diehn et al., (2002, PNAS 99:11796-11801).

As indicated above, solely to expedite prosecution of the present application, Applicants have amended claim 1 to incorporate the limitation of claim 27, which was not rejected as being obvious over Roncarolo et al. in view of Diehn et al.

Specifically, amended claim 1 recites that the culture-expanding step includes "activating the isolated CD4<sup>+</sup>CD25<sup>+</sup> cells with beads coated with anti-CD3 and anti-CD28 antibodies at a ratio of a higher amount of anti-CD28 antibody to anti-CD3 antibody".

In view of this amendment, Applicants respectfully submit that claim 1, the only independent claim pending and under examination in the present application, is not anticipated or rendered obvious by Roncarolo et al. in view of Diehn et al. Withdrawal of this rejection is thus respectfully requested.

Rejection of claim 1 for Nonstatutory Obviousness-type Double Patenting

The Examiner has provisionally rejected claim 1 under 35 U.S.C. §101 on the grounds of nonstatutory obviousness-type double patenting. The Examiner is of the opinion that claim 1 is unpatentable over claims 1-3, 10 and 14 of copending Application No. 11/226,168.

Applicants thank the Examiner for placing this rejection in abeyance until claims have actually issued or are deemed allowable in this application or copending Application No. 11/226,168.

Summary

Applicant respectfully submits that each rejection of the Examiner to the claims of the present application has been overcome or is now inapplicable, and that the claims are now in condition for allowance. Reconsideration and allowance of these claims is respectfully requested at the earliest possible date.

Respectfully submitted,  
BRUCE BLAZAR ET AL.,

SEPTEMBER 18, 2007  
(Date)

By:

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